

APPENDIX A**Claims 1-8. (Canceled)**

9. **(Previously presented)** An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1×10^{-10} M or less and a k_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance.

10. **(Previously presented)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} \text{ s}^{-1}$ or less.

11. **(Previously presented)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} \text{ s}^{-1}$ or less.

142. **(Previously presented)** The isolated human antibody, or antigen-binding portion thereof, of claim 9, which is a recombinant antibody, or antigen-binding portion thereof.

143. **(Previously presented)** The isolated human antibody of any one of claims 9 to 11, wherein the antibody is a neutralizing antibody.

144. **(Currently amended)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* phytohemagglutinin blast proliferation assay (PHA assay) with an IC_{50} of 1×10^{-7} M or less.

145. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-8} M or less

12. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less.

13. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

14. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

146. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-10} M or less.

147. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-11} M or less.

148. **(Previously presented)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 5×10^{-12} M or less.

Claims 15-40. (Canceled)

41. **(Original)** An isolated human antibody, or an antigen-binding portion thereof, which

- a) inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

149. **(Previously presented)** The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

150. **(Previously presented)** The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

42. **(Original)** The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 27; and a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 28.

43. **(Original)** The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 29; and a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 30.

44. **(Original)** An isolated human antibody, or an antigen-binding portion thereof, having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 31, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 32.

45. **(Original)** The isolated human antibody of claim 44, comprising a heavy chain constant region selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.

46. **(Original)** The isolated human antibody of claim 45, wherein the antibody heavy chain constant region is IgG1.

47. **(Original)** The isolated human antibody of claim 44, which is a Fab fragment.

48. **(Original)** The isolated human antibody of claim 44, which is a $F(ab')_2$ fragment.

49. **(Original)** The isolated human antibody of claim 44, which is a single chain Fv fragment.

Claims 50-87. **(Canceled)**

88. **(Currently amended)** A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim 9, ~~or 41, 151, 153, 164, 167, 168, or 183,~~ and a pharmaceutically acceptable carrier.

89. **(Currently amended)** The pharmaceutical composition of claim 88, which further comprises an additional therapeutic agent wherein said additional agent comprises a therapeutic agent for the treatment of an inflammatory disease or an autoimmune disease.

90. **(Canceled)**

91. **(Currently amended)** The pharmaceutical composition of claim 89, wherein the additional therapeutic agent, is selected from the group consisting of budenoside, ~~epidermal growth factor~~, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, ~~lipoxigenase inhibitors~~, mesalamine, olsalazine, balsalazide, antioxidants, ~~thromboxane inhibitors~~, antibodies to IL-1 receptor ~~antagonists~~, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, ~~growth factors~~, ~~elastase inhibitors~~, pyridinyl-imidazole compounds, anti-TNF antibodies, anti-LT antibodies, anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, anti-CD90 antibodies, ~~antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands,~~

methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, non-steroidal anti-inflammatory drugs (NSAIDs), ibuprofen, corticosteroids, prednisolone, ~~phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TNF α converting enzyme inhibitors, T cell signalling inhibitors, metalloproteinase inhibitors~~, sulfasalazine, azathioprine, 6-mercaptopurines, ~~angiotensin converting enzyme inhibitors, soluble cytokine receptors~~, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, and TGF β .

92. (Previously presented) The pharmaceutical therapeutic composition of claim 89, wherein the additional therapeutic agent is selected from the group consisting of anti-TNF antibodies, and antibody fragments thereof, TNFR-Ig constructs, ~~FACE inhibitors, PDE4 inhibitors~~, corticosteroids, budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, ~~IL-1 β converting enzyme inhibitors~~, IL-1ra, ~~tyrosine kinase inhibitors~~, 6-mercaptopurines and IL-11.

175 (New) The pharmaceutical composition of claim 89, wherein the inflammatory disease is selected from the group consisting of rheumatoid arthritis, a Crohn's disease, psoriasis, and inflammatory bowel disease (IBD).

176. (New) The pharmaceutical composition of claim 175, wherein the additional therapeutic agent for the treatment of rheumatoid arthritis is selected from the group consisting of corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), cytokine suppressive anti-inflammatory drugs (CSAIDs), anti-TNF antibodies, anti-LT antibodies, anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, anti-CD90 antibodies, anti-gp39 antibodies, or anti-CD40L antibodies.

177. (New) The pharmaceutical composition of claim 175, wherein the additional therapeutic agent for the treatment of rheumatoid arthritis is selected from the group consisting of methotrexate, leflunomide, cyclosporine, MP, azathioprine, sulfasalazine, mesalazine, olsalazine, chloroquine/hydroxychloroquine, penicillamine, aurothiomalate, azathioprine, cochlamine, corticosteroids, salbutamol, terbutaline, salmeterol, theophylline, aminophylline, cromoglycate, nedocromil, ketotifen, ipratropium and oxitropium, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, ibuprofen, prednisolone, anti-TNF α antibodies, anti-IL-1 antibodies, anti-IRAK antibodies, anti-NIK antibodies, anti-IKK antibodies, anti-p38 antibodies, Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), sulfasalazine, azathioprine, 6-mercaptopurines, p75TNFRIgG (EnbrelTM), p55TNFRIgG (Lenercept), sIL-1RI, sIL-1RII, sIL-6R, soluble IL-13 receptor (sIL-13)), IL-4, IL-10, IL-11, IL-13 and TGF β .

178. (New) The pharmaceutical composition of claim 175, wherein the additional therapeutic agent for the treatment of inflammatory bowel disease is selected from the group consisting of budenoside, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, mesalamine, olsalazine, balsalazide, antioxidants, anti-IL-1 receptor antibodies, anti-IL-1 β antibodies, anti-IL-6 antibodies, pyridinyl-imidazole compounds, anti-TNF antibodies, anti-LT antibodies, anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, anti-CD90 antibodies, anti-gp39 antibodies, anti-CD40L antibodies, methotrexate, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, corticosteroids, Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), sulfasalazine, azathioprine, 6-mercaptopurines, p75TNFRIgG (EnbrelTM),

p55TNFRlgG (Lenercept), soluble IL-1RI, soluble IL-1RII, soluble IL-6R, soluble IL-13 receptor (sIL-13)), IL-4, IL-10, IL-11, IL-13 and TGF β .

179. (New) The pharmaceutical composition of claim 175, wherein the additional therapeutic agent for the treatment of Crohn's disease is selected from the group consisting of anti-TNF antibodies, D2E7, cA2 (Remicade™, CDP 571, anti-TNF antibody fragments, p75TNFRlgG (Enbrel™) and p55TNFRlgG (Lenercept)), anti-P7s, p-selectin glycoprotein ligand (PSGL), soluble IL-13 receptor (sIL-13), budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, anti-IL-1 antibodies, Vx740, and 6-mercaptopurines.

180. (New) The pharmaceutical composition of claim 89, wherein the autoimmune disease is multiple sclerosis.

181. (New) The pharmaceutical composition of claim 180, wherein the additional therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a (Avonex), interferon- β 1b (Betaseron), Copolymer 1 (Cop-1; Copaxone), hyperbaric oxygen, clabribine, anti-TNF antibodies, anti-LT antibodies, anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, anti-CD90 antibodies, anti-gp39 antibodies, anti-CD40L antibodies, methotrexate, cyclosporine, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), sulfasalazine, azathioprine, 6-mercaptopurines, soluble p55, soluble p75 TNF receptors, soluble IL-1RI, soluble IL-

IRII, soluble IL-6R, soluble IL-13 receptor (sIL-13), IL-4, IL-10, IL-11, IL-13 and TGF β . IFN β 1a, IFN β 1b, copaxone, and IL-1.

182. **(New)** The pharmaceutical composition of claim 88, which further comprises an additional therapeutic agent for the treatment of insulin dependent diabetes mellitus.

93-141 **(Canceled)**

151. **(Previously presented)** An isolated human antibody, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K_d of 1×10^{-10} M or less and binds to an epitope on the p40 subunit of human IL-12.

152. **(Previously presented)** The isolated human antibody of claim 151, which neutralizes the activity of human IL-12.

153. **(Previously presented)** A neutralizing isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-3} s^{-1}$ or less, as determined by surface plasmon resonance.

154. **(Previously presented)** The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} s^{-1}$.

155. **(Previously presented)** The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} s^{-1}$ or less.

156. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-7} M or less

157. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-8} M or less.

158. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less.

159. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

160. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

161. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC_{50} of 1×10^{-10} M or less.

162. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC_{50} of 1×10^{-11} M or less.

163. **(Previously presented)** The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC_{50} of 5×10^{-12} M or less.

164. **(Previously presented)** An isolated human antibody, or an antigen-binding portion thereof, which

- a) dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

165. **(Previously presented)** The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} \text{ s}^{-1}$ or less.

166. **(Previously presented)** The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} \text{ s}^{-1}$ or less.

167. **(Previously presented)** An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and comprises:
a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and
a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

168. **(Previously presented)** An isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26, and with a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

169. **(Previously presented)** The isolated human antibody, or an antigen-binding portion thereof, of claim 168, wherein the LCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 28 and the HCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 27.

170. **(Previously presented)** The isolated human antibody, or an antigen-binding portion thereof, of claim 169, wherein the LCVR further has CDR1 domain comprising

the amino acid sequence of SEQ ID NO: 30 and the HCVR has a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 29.

171. **(Previously presented)** A pharmaceutical composition comprising an antibody or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody comprises:

a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and

a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

172. **(Previously presented)** An isolated human antibody that binds human IL-12 and is the antibody J695, or an antigen binding portion thereof.

173. **(Previously presented)** A pharmaceutical composition comprising the isolated human antibody of claim 172 and a pharmaceutically acceptable carrier.

174. **(Currently amended)** The pharmaceutical composition of claim 173, which further comprises at least one additional therapeutic agent, wherein said agent comprises a therapeutic agent for the treatment of an inflammatory or an autoimmune disease.

183. **(New)** An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1.34×10^{-10} M or less, and neutralizes human IL-12.

184. **(New)** The isolated human antibody of claim 183, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K_d of 9.74×10^{-11} M or less

185. **(New)** The isolated human antibody, or antigen-binding portion thereof, of claims 183 or 184, which is a recombinant antibody, or antigen-binding portion thereof.

186. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-7} M or less.

187. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-8} M or less.

188. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less.

189. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

190. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

191. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-10} M or less.

192. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 1×10^{-11} M or less.

193. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human $IFN\gamma$ production with an IC_{50} of 5×10^{-12} M or less.

194. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC_{50} of 1×10^{-9} M or less.

195. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC_{50} of 1×10^{-10} M or less.

196. (New) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC_{50} of 1×10^{-11} M or less.